REMARKS

Claims 49-73 were under examination as of the issuance of the Office Action of February 7, 2006. By the current Amendment to Claims, claims 49-51 have been amended.

Support for the amendments to the claims can be found throughout the specification and in the claims as originally filed. Specifically, support for the amendment to claims 50 and 51 can be found throughout the specification, for example, at page 32, line 16 to page 35 line 10, and in the claims as originally filed, for example, claim 49.

Applicants respectfully request that the aforementioned amendments be entered. No new matter has been added by the foregoing amendments. Applicants note that the foregoing amendments and cancellation of claims have been made solely in order to expedite examination and in no way should be construed as an acquiescence to the validity of the rejections set forth in the Office Action. Following entry of the foregoing amendments, claims 49-73 will remain pending in the present application.

Withdrawal of Claims 57-59, 63-64 and 67-68

Applicants acknowledge the election of Group 142 (*i.e.*, claims 49-51 drawn to a peptide of formula V/SEQ ID NO:293) and the species of SEQ ID NO:295 as set forth in the Responses to Restriction Requirement of November 9, 2005 and November 29, 2005.

In the Office Action, claims 57-59, 63-64 and 67-68 were withdrawn from consideration on the ground that

> [t]he elected species SEQ ID NO:295 was found free of the art and allowable. The search was extended to other members of the genus for which prior art was found. Those claims that do not read on the anticipated species are withdrawn from consideration; claims 57-59, 63-64 and 67-68 are withdrawn.

Applicants respectfully traverse the withdrawal of these claims. Applicants assert that the withdrawal of the allowable claims is improper, as set forth in MPEP § 809.02(c). Applicants assert that under standard restriction practice, those species claims that are free of the prior art should be deemed allowable and not withdrawn. As set forth in MPEP § 809.02 and under standard restriction practice, an applicant is required to "elect a species of his or her invention to which his or her claim will be restricted if no claim to the genus is found to be

allowable." Indeed, allowable species claims should not be withdrawn; instead, such claims should be deemed allowable. Accordingly, Applicants respectfully request reconsideration of the withdrawal of claims 57-59, 63-64 and 67-68.

Claim Objections

Claim 50 has been objected to as "fail[ing] to recite 'formula V.'" Solely in the interest of expediting examination, Applicants have amended claim 50 to recite "formula V," thereby rendering the foregoing objection moot.

In addition, claims 71-73 have been objected to

> for the recitation of amino acid sequences that do not fit the elected subject matter or the species to which art is presently applied (see for example SEQ ID NOs: 296, 298-299, 301-320, 322-323, 325-326, 328-347, 349-350, 352-353, 355-376).

Applicants traverse the foregoing objection. Applicants submit that each of the amino acid sequences set forth in claims 71-73 fall within the subject matter of Group 142 (*i.e.*, claims 49-51 drawn to a peptide of formula V/SEQ ID NO: 293). Indeed, each of the recited amino acids set forth in claims 71-73 are exemplary of formula V, *i.e.*, $RX_6X_7X_8X_9$ as defined in claims 49-51, as originally presented. Moreover, with respect to the assertion that "the amino acid sequences do not fit within the elected subject matter or the species to which the art is presently applied," Applicants submit that under standard restriction practice as applied in the examination of the present application, it is unnecessary for the claims to be limited to a particular species. Indeed, the election of a particular species in the present application is for search purposes only. Accordingly, because the sequences of claims 71-73 fall within the scope of the elected Group 142, *i.e.*, a peptide of formula V, and further because limitation to a particular species is unnecessary, Applicants submit that claims 71-73 are in proper form. Applicants respectfully request reconsideration of the objection of claims 71-73.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the objections of claims 50 and 71-73.

Rejection of Claims 50-56, 60-62, 65-66 and 69-70 under 35 USC § 112

Claims 50-56, 60-62, 65-66 and 69-70 have been rejected under 35 USC § 112, second paragraph, "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention."

Specifically, claims 49-51 have been rejected "because it is unclear as to whether the claims are open or closed language regarding whether the formula V is limited to consisting of the penta-peptide or is merely comprising the penta-peptide." Solely in order to expedite examination and in no way acquiescing to the validity of the rejection, Applicants have amended claims 49 to recite "consisting of the formula," thereby rendering the foregoing rejection moot.

In addition, claims 50-56, 60-62, 65-66 and 69-70 have been rejected "for the recitation of limitations on specific amino acid residues that are not defined in the base claims. Claims 50 and 51, for example, lack definitions to the X residues in the claimed formula; thus, all subsequently dependent claims are adding limitations on undefined amino acid residues and themselves are indefinite limitations." In order to expedite examination, Applicants have amended claims 50 and 51 to further define the "X" amino acid residues, thereby rendering the foregoing rejection moot.

In view of the foregoing amendments, Applicants respectfully request reconsideration and withdrawal of the foregoing rejections under 35 USC § 112, second paragraph.

Rejection of Claims 49-56, 60-62, 65-66 and 69-71 Under 35 U.S.C. § 102(b) and 102(e)

Claims 49-56, 60-62, 65-66 and 69-71 have been rejected under 35 U.S.C. § 102(b) as being anticipated by WO97/42222 to Ball *et al.* (hereinafter referred to as "Ball") on the ground that Ball

> teaches the species RRLIF (page 63, lines 16-19). This species meets the and anticipates the limitations of the instant claims 49-56, 60-62, 65-66, 69-71, additionally, '2222 teaches many variants, i.e., page 75 line 20, of the instantly claimed formulas as applied by the variant definitions in the instant specification.

In addition, claims 49-56, 60-62, 65-66 and 69-71 have been rejected under 35 U.S.C. § 102(e) as being anticipated by US Patent No. 6,962,792 to Ball *et al.* (hereinafter referred to as the "'792 patent") on the ground that the '792 patent

> teaches the species RRLIF (SEQ ID NO:12) which meets the limitations of the instant claims 49-56, 60-62, 65-66, 69-71. Additionally, the '792 patent teaches variants of the

> RRLIF penta-peptide as they are described in the instant specification, wherein the variants of peptide formula V are 'modified by at least one of a deletion, addition or substitution of one or more amino acid residues' at pate [sic] 32, lines 25-31.

Initially, Applicants note that the '792 patent is a national phase application of International Publication No. WO97/42222 under 35 U.S.C. § 371 and, as such, the teachings of each reference are substantially identical. Accordingly, Applicants will address both rejections together in the following discussion.

Applicants respectfully traverse the foregoing rejections. The presently claimed invention is a pentamer peptide sequence of 5 residues, as defined by the closed language "consisting of." The claimed sequences are thus limited as such, and do not include larger peptide fragments including the residues $RX_6X_7X_8X_9$. Accordingly, Applicants submit that neither of the cited references disclose a pentapeptide ***consisting of*** the amino acid sequences $RX_6X_7X_8X_9$ as set forth in the pending claims.

Indeed, the RRLIF motif taught by Ball is a ***predicted structural motif identified within larger p21 fragments***. First, Ball arrived at the predicted structural motif by synthesizing a series of peptides shifted by 4 amino acids in either direction of peptide 10 (KRRQTSMTDFYHSKRRLIFS), *i.e.*, by performing a size scan. As set forth in Figure 5, and further described at page 44, line 26 to page 45, line 3, each of these peptides was a 20 mer, except peptide g which was a 16 mer. Second, Ball arrived at the predicted structural motif by synthesizing a series of peptides based on peptide 10, in which each residue is sequentially mutated to alanine and the activity of the resulting peptides were assessed. In each case, as depicted in Figure 6 and further described on page 45, lines 5-17, each peptide was a 20 mer. Ultimately, Ball concluded that the RRLIF motif is important for inhibitory activity, but at no point did Ball synthesize or describe the isolated pentapeptide RRLIF. Indeed, the shortest sequence described in Ball was an 8 mer (KRRLIFSK) peptide (see page 65, line 28).

The Office Action cites page 63, lines 16-19 of Ball as teaching the claimed invention. However, this excerpt cited by the Examiner is in the midst of Ball's discussion of the alanine mutation method described above and as set forth in Figure 6, each of the resulting peptides tested by Ball in this experiment contained 20 amino acids. Further in support of the rejection, the Office Action cites SEQ ID NO:12 of the '792 patent. However, the RRLIF sequence disclosed in SEQ ID NO:12 of this patent is described as a "Description of Artificial Sequence:

Motif," in contrast to the other sequences which are described as "Synthesized." Indeed, the RRLIF pentamer peptide was not synthesized or described by Ball; instead, the sequence was elucidated as a motif of a larger p21 fragment.

Accordingly, Applicants submit that the teachings of Ball fail to teach each and every limitation of the claimed invention, *i.e.*, a peptide ***consisting of*** the amino acid sequences $RX_6X_7X_8X_9$ and, therefore, Applicants respectfully request reconsideration and withdrawal of the rejections of claims 49-56, 60-62, 65-66 and 69-71 under 35 U.S.C. § 102(b) as being anticipated by Ball and under 35 U.S.C. § 102(e) as being anticipated by the '792 patent.

Rejection of Claims 49-56, 60-62, 65-66 and 71-73 Under 35 U.S.C. 103(a)

Claims 49-56, 60-62, 65-66 and 71-73 have been rejected under 35 U.S.C. 103(a) as being obvious over Ball on the grounds that

> [a]t page 5, lines 17-21 and at pages 79-80, '2222 teaches the formula xyLzF, wherein x is Arginine and y and z are any amino acid. This formula and the limitations on the open residues renders obvious many variants and sequences of the instantly claimed formula V sequence of claims 49-56, 60-62, 65-66, 71-71, i.e. SEQ ID NOs: 294, 297, 300, 321, 324, 327, 348, 351, 354 and 377 of claims 71-73.

Applicants respectfully traverse the foregoing rejection. Applicants submit that while Ball teaches a genus of pentamers, Ball fails to teach the subgenus of pentamers specifically defined by the present claims. Indeed, while Ball discloses a sequence of the formula xyLzF, Ball defines both y and z as any amino acid. In contrast, claims 49-51 specifically define the y and z residues as particular amino acids not specifically taught by the prior art. As set forth in MPEP § 2144.08, in determining whether a claimed species or subgenus would have been obvious to one of ordinary skill in the art in view of a disclosed genus, the Examiner must establish a prima facie case of obviousness in part, by demonstrating that "one of ordinary skill in the relevant art would have been motivated to make the claimed invention as a whole, *i.e.*, to select the claimed genus or subgenus from the disclosed prior art genus." Applicants submit that Ball fails to provide the motivation for a skilled artisan to arrive at the claimed subgenus of pentamers.

Applicants submit that the teachings of Ball are generally directed to sequences that are capable of interacting with CDK4/cyclin D so as to inhibit CDK4. Indeed, the various sequences taught by Ball are directed to binding and inhibiting CDK4. For example, Applicants direct the

Examiner's attention to the teachings of Ball throughout the specification, for example, at page 10, lines 10-17, the Examples and Figures 1-10, each of which assess the ability of various fragments to bind with, interact with and/or inhibit CDK4 or cyclin D. Moreover, even the excerpts cited to by the Examiner, *i.e.*, at page 5, lines 17-21 and at pages 79-80, each characterize the xyLzF sequence as a sequence for interacting or binding with cyclin D1 and CDK4.

In contrast, formula V of the present application is directed to particular sequences for specifically binding cyclin E/CDK2 and cyclin A/CDK2. Indeed, the peptides of the present invention are capable of preferentially and selectively binding CDK2 over CDK4. At page 20, lines 2-12 of the specification, Applicants teach that

> [a]lthough the peptides of the first aspect and in some embodiments of the second aspect, include the described CDK4-inhibitory motif RRLIF, the peptides of the present invention have been shown to display preferential selectivity for CDK2 over CDK4 in contrast to those described in Ball et al. [*Current Biol.* (1996) 7:71-80] who concluded that such p21 carboxy–terminal peptides 'do not have high specific activity for CDK2 inhibition, they are potent inhibitors of CDK4 activity'. Thus, Ball et al. do not focus upon this region for further development for preferential CDK2 inhibitors, indeed $p21_{141-160}$ was shown by these authors to be 40 times more active against cyclinD1/CDK4 than cyclinE/CDK2. Thus, further surprising advantages of the above peptides relate to their specificity, particularly for G1 control CDK's, such as CDK2/cyclinE and CDK2/cyclin A, as opposed to mitotic control enzymes including CDK's such as CDK1/cyclin B or A and protein kinase Cα (PKCα).

Moreover, as set forth in the preceding excerpt, the state of the art at the time, as indicated in Ball *et al.* (*Current Biol.* (1996) 7:71-80), previously submitted in an Information Disclosure Statement dated November 9, 2005, was such that a skilled artisan would conclude that p21 carboxy-terminal peptides "do not have high specific activity for CDK2 inhibition...". Accordingly, a skilled artisan would not be motivated to use carboxy terminal p21 fragments to design the subgenus of p21 fragments capable of preferentially binding with CDK2 as claimed in the present application.

In view of the teachings of Ball as focused on the design of p21 fragments capable of binding CDK4 and further in view of the state of the art as teaching that carboxy terminal p21 fragments do not preferentially bind CDK2, Applicants submit that one skilled in the art would not be motivated to search for and arrive at the claimed subgenus of molecules, as required for a

prima facie case of obviousness under MPEP 2144.08 (II)(A)(4). Accordingly, Applicants respectfully request reconsideration and withdrawal of the foregoing rejection.

Provisional Rejection Under Judicially Created Doctrine of Obviousness-type Double Patenting

Claims 49-56, 60-62, 65-66 and 70 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting "as being unpatentable over claims 16-22, 24-25, 58-64, 66, 70-78 and 80-83 of copending Application No. 09/726,470." Specifically, the Office Action sets forth that

> [t]he '470 claims are drawn to many peptide sequences that comprise the instantly claimed peptide formula V of instant claims 49-56, 60-62, 65-66, and 70, i.e. the '470 claimed sequences comprise the $-RX_4LX_5F-$-. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are drawn to various sequence possibilities and variants of peptide formula V. Due to the indefiniteness of the instant claims regarding whether the claim language is opened or closed, the instant claims are interpreted as being open language for purposes of this rejection. Therefore, the '470 claims render obvious the instant claims wherein all the required limitations are claimed. In the case that the language is to be closed by amendment, it should be noted that the claims would still render obvious variants of the instantly claimed peptide formula V.

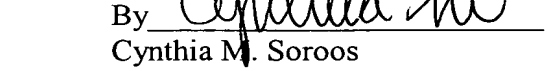
While in no way acquiescing to the Examiner's rejections under the judicially created doctrine of obviousness-type double patenting, Applicants note that prosecution of the present application and copending Application No. 09/726,470 may render such rejection moot. Accordingly, once the pending claims in the present application are formally indicated as otherwise allowable, and should such submission(s) be necessary, Applicants will submit a terminal disclaimer in compliance with C.F.R. §§ 1.321(b) and (c), as appropriate, which will obviate this rejection.

SUMMARY

Applicants respectfully submit that the above-identified application is in condition for allowance. If a telephone conversation with Applicants' attorney would expedite prosecution of the above-identified application, the Examiner is urged to call Applicants' Attorney at (617) 227-7400.

Dated: August 7, 2006

Respectfully submitted,

By 

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